Remarks

Claims 76-133 were pending in the subject application. By this amendment, applicants have canceled claims 111-113 and amended claims 100, 117 and 123. Consequently, claims 76-110 and 114-133 are currently pending.

Restriction Requirement

In the Restriction Requirement issued on March 25, 2003, the Examiner required restriction to one of the following allegedly distinct inventions as follows:

I. Claims 76-99, 103-109, and 124-132, drawn to 7-deaza-2-benzyl substituted purine compounds and pharmaceutical compositions containing same;
II. Claims 100-102 and 117-122 drawn to methods for treating a disease associated with an A3 adenosine receptor in need of such treatment;
III. Claim 110, drawn to a method for inhibiting the activity of an A3 adenosine receptor in a cell that is subjected to abnormal stimulation of the A3 adenosine receptor;
IV. Claims 111-113, drawn to methods for treating a gastrointestinal disorder associated with an A3 adenosine receptor;
V. Claims 114-115, drawn to methods for treating a respiratory disorder associated with an A3 adenosine receptor;
VI. Claims 116 and 123, drawn to methods for treating inflammation of the eyes associated with an A3 adenosine receptor;
VII. Claim 133, drawn to methods for preparing 7-deaza-2-benzyl substituted purine compounds.

The Examiner alleged that inventions I and II, III, IV, V and VI are related as product and process of use. The Examiner

maintained that the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product; or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05(h)). The Examiner alleged that in the instant case the products of Invention I may be used in materially different methods than those of Inventions II, III, IV, V or VI as evidenced by Applicant's use of the compounds in the distinct inventions of II, III, IV, V and VI. With regard to Inventions I and VII, the Examiner alleged that the inventions are distinct because the product as claimed can be made by another and materially different process (MPEP §806.05(f)). The Examiner further alleged that Inventions II, III, IV, V and VI are unrelated because they possess different functions (MPEP §806.04, MPEP §808.01). The Examiner alleged that while the function of Invention II is to treat diseases associated with A3 adenosine receptor cells, the functions of Inventions IV, V and VI, as claimed, are not limited to treatment of diseases associated with A3 adenosine receptor cells. Specifically, the Examiner alleged, the functions of Inventions IV, V and VI are treating of gastrointestinal disorders, respiratory disorders and damage to the eye, respectively, neither of which need be A3 adenosine related. Additionally, the Examiner alleged that the Inventions produce different effects. The Examiner therefore concluded that restriction for examination purposes is deemed proper.

In response, applicants hereby elect, with traverse, Group I for the purposes of preliminary examination.

Applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement in its entirety. Applicants contend that Groups I-VII do not constitute independent and distinct inventions. In fact, every claim of alleged Groups II-

VII depends on or otherwise incorporates the limitations of the claims of Group I. Applicants draw the Examiner's attention to 37 C.F.R. §1.141(b) which states:

> Where claims to all three categories, product, process of making, and process of use, are included in a national application, a three way requirement for restriction can only be made where the process of making is distinct from the product. If the process of making and the product are not distinct, the process of using may be joined with the claims directed to the product and the process of making the product even though a showing of distinctness between the product and process of using the product can be made. (Emphasis added)

Applicants' claimed process is specifically directed to making the claimed product and cannot be used to make a different product. The Examiner has not shown how the claimed product can be made in a different process. Consequently, restriction in the present application between Groups I, II, III, IV, V, VI, and VII is not proper under 37 C.F.R. §1.141(b).

In addition, applicants contend that the Examiner has not satisfied the requirements of M.P.E.P. 806.05(f) with respect to the restriction of Group VII. M.P.E.P. Section 806.05(f) states:

> A process of making and a product made by the process can be shown to be distinct inventions if either or both of the following can be shown: (A) that the process *as claimed* is not an obvious process of making the product and the process as claimed can be used to make other and different products; or (B) that the product as claimed can be made by another and materially different process.

Applicants note that the Examiner has failed to show that either

of these two requirements has been satisfied. Clearly the recited process cannot be used to make other products because only the products of Group I are recited. The Examiner also has not provided any different process for making the products. Consequently, the Examiner's restriction to Group VII is not supported by M.P.E.P. 806.05(f), is improper, and should be withdrawn.

On page 3 of the March 25, 2003 Office Action, the Examiner asserted that M.P.E.P. 806.05(h) supports the restriction of Groups II-VI from Group I. Applicants contend that the Examiner has not satisfied the requirements of M.P.E.P. 806.05(h). M.P.E.P. 806.05(h) states:

> A product and a process of using the product can be shown to be distinct inventions if either or both of the following can be shown: (A) the process of using as claimed can be practiced with another materially different product; or (B) the product as claimed can be used in a materially different process.
>
> The burden is on the examiner to provide an example, but the example need not be documented.
>
> If the applicant either proves or provides a convincing argument that the alternative use suggested by the examiner cannot be accomplished, the burden is on the examiner to support a viable alternative use or withdraw the requirement. (Emphasis added)

The Examiner alleged that the products of Invention I may be used in materially different methods than those of Inventions II-VI. However, the Examiner failed to provide an example of any such use. The only evidence offered by the Examiner is "applicant's use of the compounds in the distinct inventions of II, III, IV, V and VI." Applicants find this reasoning circular and confusing. The fact that applicants claim the use of the compounds in claims

belonging to allegedly distinct inventions II-VI does not show an "alternative use." Applicants' claims in Groups II-VI all follow from the compounds' A3 adenosine receptor antagonist activity, i.e. a single activity to which the Examiner has offered no "alternative." The mere statement by the Examiner that the compounds may be used in materially different methods is insufficient basis on which to ground a restriction. Thus, applicants contend that the restriction between Inventions I and II-VI is improper pursuant to M.P.E.P. 806.05(h).

Applicants point out that the claims of Groups II-VI are only claiming one specific use, namely, inhibition of the A3 adenosine receptor. The effect of treatment with the compounds of the invention is the inhibition of the A3 adenosine receptor and this effect is the same for all the allegedly distinct Inventions. This inhibition, however, has multiple secondary effects. Specifically, inhibiting the A3 adenosine receptor results in treatment of the symptoms of the diseases claimed in the subject application. Thus, inhibition of only one receptor (A3), e.g. one utility, results in the treatment of a number of A3 related disorders.

Furthermore, the functions of Inventions IV, V and VI do not include treatment of gastrointestinal disorders, respiratory disorders or damage to the eye which are not related to the A3 adenosine receptor, as the Examiner alleged. Applicants point out that each of claims 111, 114 and 116 recites the limitation "associated with an A3 adenosine receptor." Consequently, treatment of diseases which are not associated with the A3 adenosine receptor are not encompassed by the claims of the subject invention. Thus, applicants contend that Inventions II-VI are related and not distinct and consequently restriction is improper.

With regard to the restriction between Inventions III and II, IV-VI, applicants are unclear as to what the Examiner intended in her argument. The Examiner alleged that "While the function of Invention II is to treat diseases associated with A3 adenosine receptor cells, the functions of Inventions IV, V and VI, as claimed, are not limited to treatment of diseases associated with A3 adenosine receptor cells." Applicants point out that the A3 adenosine receptor is always located on a cell. Consequently, diseases associated with the A3 adenosine receptor are, by definition, associated with cells which possess the A3 adenosine receptor (i.e. A3 adenosine receptor cells). Accordingly, applicants contend that the restriction between Inventions II-VI is improper and should be withdrawn.

Furthermore, applicants note that M.P.E.P. §806.05(h) does not address how to treat such claims once a product claim is allowed. M.P.E.P. § 806.05(i) addresses how to treat such claims once the product claim is allowed:

> Where the product claims are allowable (i.e., novel and nonobvious), restriction may be required only where the process of making and the product made are distinct (MPEP § 806.05(f)); otherwise, *the process of using must be joined with the process of making and product made, even if a showing of distinctness can be made between the product and process of using* (MPEP § 806.05(h)). (Emphasis added)

Indeed, such treatment of the claims is rational in view of the minimal burden on the Examiner to examine process of use claims which incorporate all of the limitations of an allowed product claim. Consequently, applicants maintain that even if the restriction of Invention I from Inventions II-VI is maintained

for the purpose of preliminary examination, Inventions II-VI should be rejoined and examined once the product claims are found allowable.

In addition, applicants point out that claim 76 is a linking claim that links the inventions of Groups I-VII according to M.P.E.P. § 809.03. Pursuant to M.P.E.P. § 809.04 "*[I]f a linking claim is allowed, the examiner must thereafter examine* species if the linking claim is generic thereto, or he or she must examine *the claims to the nonelected inventions that are linked* to the elected invention by such allowed linking claim." (Emphasis added). Therefore, applicants hereby respectfully request that the Examiner examine nonelected Inventions II-VII once the linking claim of Invention I is found allowable.

In view of the preceding discussion, applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement in its entirety.

THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed on Form PTO-1449 (**Exhibit A**) and are also listed below. Copies of the references listed below as items 1-3 are attached hereto as **Exhibits 1-3**.

This Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3) before the mailing of a first Office Action on the merits. Thus, this Information Disclosure Statement should be entered and considered.

Applicants also point out that the references disclosed in this Information Disclosure Statement were first cited in an EPO

Search Report dated March 28, 2003 in a corresponding EPO application not more than three months prior to the filing of the subject Information Disclosure Statement. A copy of the March 28, 2003 EPO Search Report is attached hereto as **Exhibit B**.

1. Campbell, R.M. et al., "Selective A_1-Adenosine Receptor Antagonists Identified Using Yeast *Saccharomyces Cerevisiae* Functional Assays" *Bioorg. & Med. Chem. Lett.* (1999) 9(16): 2413-2418 (**Exhibit 1**);

2. Zhao, Z. et al., "Bioactivation of 6,7-Dimethyl-2,4-di-1-pyrrolidinyl-7H-pyrrolo[2,3-d]pyrimidine (U-89843) to Reactive Intermediates that Bind Covalently to Macromolecules and Produce Genotoxicity" *Chem. Res. Toxicol.*, (1996) 9: 1230-1239 (**Exhibit 2**); and

3. Dhainaut, A. et al., "New Purines and Purine Analogs as Modulators of Multidrug Resistance" *J. Med. Chem.* (1996) 39: 4099-4108 (**Exhibit 3**).

Applicants request that the Examiner review the references and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment and Response to Restriction Requirement with Third Supplemental Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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